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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,955	12/13/2001	James R. Lupski	HO-P02086US1	2699

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,955	LUPSKI ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,35-40 and 42-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,35-40 and 42-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action and amendment filed on January 9, 2004 has been entered and considered.

2. The Declaration under 37 CFR 1.132, submitted on January 9, 2004 is entered.

3. Claims 1, and 35 are amended, claims 8-34, 41 are canceled. New claims 43-50 are added. Claims 1-7, 35-40, 42-50 are currently pending in this application.

4. This application has a filing date as December 13, 2001 and claims priority to US provisional application 60/255,217 filed on 12/13/2000. MPEP. 02-10 notes that

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Upon verification of the provisional application 60/ 255,217, it is noted that the disclosure is not the same as the instant application. SEQ ID No. 76 and the specific nucleotide alteration 247ΔC do not get the benefit of the prior application because the provisional application does not disclose the sequence of SEQ ID No.76 and the mutation at 247ΔC.

Response to arguments

5. Applicants' arguments and amendment have been fully considered and found persuasive in part.

6. With reference to the objection to the instant specification regarding the uses of embedded hyperlink, Applicants' amendment is fully considered and the objection is withdrawn herein.

7. With reference to the objection to the instant specification regarding defective Oath / Declaration, the objection is withdrawn herein. Applicants correctly pointed out that the objection was an error and examiner recognizes that it was indeed an error.

8. With regard to the election of one SEQ ID No., Applicants' arguments are fully considered and found not persuasive because as discussed in the restriction requirement, examiner reinstates that this is NOT an election of species. Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequences are presumed to represent an independent and distinct invention, subject to restriction requirement pursuant to 35 USC 121 and 37 CFR 1.141. By statute, "[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions." 35 U.S.C. 121. Pursuant to this statute, the rules provide that "[i]f two or more independent and distinct inventions are claimed in a single application, the examiner in his action shall require the applicant to elect that invention to which his claim shall be restricted." 37 CFR 1.142 (a). See also 37 CFR 1.141(a). This restriction is made FINAL.

9. With regard to the arguments regarding claim 2 and 6, the arguments are fully considered, and claims are considered for examination herein. The rejection under 35 USC 112, first paragraph is rewritten herein including the claims 2 and 6. Accordingly this office action is Non-Final.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 35-40 and 42-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (see In re Wands, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

Quantity of Experimentation Necessary

Amount of Direction and Guidance

Presence and Absence of Working Examples

Nature of Invention

Level of Predictability and unpredictability in the art

Nature of the Invention :

Claims 1-7 are drawn to a method of diagnosing myelinopathy in an individual and claims 35-40, and 42 are drawn to a method of detecting the presence or absence of any mutation in a periaxin polynucleotide and its association with any myelinopathy. Further, Claim 7 is drawn to a specific alteration in a periaxin polynucleotide and Claim 36 is drawn to an association

between a specific mutation in periaxin and any myelinopathy. Claims 4 and 40 are broadly drawn to a broad range of diseases of myelinopathy such as Charcot-Marie-Tooth (CMT) syndrome, hereditary neuropathy with liability to pressure palsies (HNPP), Dejerine-Sottas syndrome (DSS), congenital hypomyelinating neuropathy (CHN), and Roussy-Levy syndrome (RLS).

Amount of Direction and Guidance:

The specification discloses the identity of several mutations in periaxin polynucleotide and their locations (see Figs. 4 and 9). The specification on page 14, asserts a correlation between the human orthologue of murine and rat periaxin (Prx) with human inherited myelinopathy and further asserts that human periaxin gene which encodes two PDZ domain proteins, is required for the maintenance of peripheral nerve myelin. The specification teaches that based on knockout animal models, periaxin is correlated to the proper formation of myelin sheaths and the specification broadly discloses the identification of recessive Prx mutations comprising nonsense and frame shift mutations in the periaxin gene. The specification asserts that based on the common known methods in the art, mutations in other periaxin polynucleotide sequences (for example SEQ ID No. 76) could be detected. The specification discloses mutations in SEQ ID No.1 and extrapolates the use of similar techniques to detect mutations in other periaxin polynucleotides (for example SEQ ID NO.76). The specification discloses mutations in other genes associated with some myelinopathy (see page 20) (such as DNA rearrangements in CMT patients caused by mutations in MPZ, Cx32, EGR2, and mutations in MPZ and EGR2 in DSS patients). Further the specification on page 21, asserts the function of periaxin in the maintenance of the myelin sheath based on animal studies. However, the specification has not established that

a statistically significant association exists between all of the specific mutations disclosed in the specification, and any myelinopathy, or any specific myelinopathy, or that a predictable correlation can be made as to an association between any mutation in the periaxin gene and any mylenopathy or any specific myelinopathy.

Presence and Absence of working examples:

The specification discloses a method of screening Prx mutations in some family studies and detected mutations comprising a deletion and a transition in the affected patients with peripheral neuropathy. The specification correlates the mutations with the loss of function of Prx gene in relation to studies in rat (example 4). The examples 2-4 in the specification establish a positive correlation between the presence of a periaxin polynucleotide comprising mutation which results in a truncated periaxin polypeptide in patients with undisclosed myelinopathy, wherein said patients have two aberrant forms of periaxin polypeptides. Although the specification does not demonstrate such, the specification asserts that the mutations could be associated with loss of function of the periaxin polypeptide. It is noted, however, that these examples also establish that the mere presence of a mutation (i.e., only a single copy) is NOT associated with the disease as in HOU579 family, wherein the unaffected parents had a single mutant polynucleotide and a wild type polynucleotide. Further there is no description of the type of peripheral neuropathy of the affected patients. (see page 65, example 3). Further examples in the specification merely assert s correlation between mutations in Prx with myelinopathy in general, however no specific mutation is associated with any of the different types of myelinopathies as exemplified by the example 8 in the specification (see page 72). Further table- 2 shows that the unaffected control subjects contain mutations in periaxin. The specification does not teach whether the mutations in

table-2 are associated with loss of function or if they are statistically associated with any specific peripheral neuropathy or any specific myelinopathy.

Level of Predictability and unpredictability in the art :

Predictability in the art suggests mutations in genes other than the specific periaxin gene, are associated with specific type of myelinopathy, for example Boss et al. (USPN. 5,691,144) teaches mutations in connexin-32 are associated with X-linked Charcot-Marie-Tooth (CMT) disease, Timmermann et al. (Neurology, Vol. 52, pp. 1827-1832, 1999) teach a missense mutation in EGR2 gene in association with Dejerine-Scottas syndrome (DSS). Lupski et al. (USPN. 5,780,223) teach DNA duplication in CMT1A gene sequence association with autosomal dominant CMT disease, and Roa et al. (Nature Genetics, Vol. 5, pp. 269273, 1993) teach that some point mutations in peripheral myelin protein 22 (PMP22) gene are associated with CMT1A, while others are associated with DSS (Fig.3, page 271). With regards to the specific periaxin gene Guilbot et al. (Human Molecular Genetics, Vol. 10, No.4, 2001), teach periaxin is responsible for CMT4F, an autosomal recessive form of CMT disease, and Gillepsie et al. (Neuron, Vol. 12, pp. 497-508, 1994) teach role of periaxin in rat pheripheral nervous system and discloses that periaxin localization in schwann cells and its possible role in ensheathment. However, the art does not establish a predictable association that any specific mutation in periaxin or any other genes is predictably associated with all of the large number of diseases encompassed by the recitation of "myelinopathy". For example Roa et al. teach that while some point mutations in PMP22 are associated with CMT1A, others are associated with DSS. Further, while Boerkoel et al. (Am. J. Hum. Genet., Vol. 68, pages 325-333, 2001) teach that certain specific mutations are associated with DSN, when both copies of periaxin gene are

altered, Boerkoel et al. further teach that the family members with only one altered copy of periaxin gene were not affected and also teach a number of missense mutations in normal and unaffected family members. The art is further silent with regard to a predictable association between any specific mutation in periaxin and a representative number of diseases encompassed by the term "myelinopathy". Diseases encompassed by the term "myelinopathy" include a large number of heterogeneous diseases with differing symptoms and associations to genetic mutations. To date, however, there is no evidence that the association of a mutation in a specific gene and a specific form of myelinopathy can predictably correlate the presence of any other, or all, specific myelinopathy encompassed by the broad term "myelinopathy". The claims further broadly encompass detecting an association between any specific mutation in periaxin, and an association to a specific unnamed myelinopathy. The specification, however does not establish a statistically significant association with any of the disclosed mutations in periaxin, and any specific form of myelinopathy such that the skilled artisan might be able to predictably correlate which mutations in periaxin would be associated with a specific form of myelinopathy. Furhter, to date, no teaching is available in the art with regards to a universal correlation between any mutation in periaxin and an association with any general or specific type of myelinopathy. It is apparent from the prior art that the unpredictability is high and the instant specification fails to teach any particular mutation associated with any particular type of myelinopathy. Given the broad scope of the claims, the specification does not provide any specific example that would easily predict a significant association of any particular mutation in periaxin with any particular type of myelinopathy. Further, CMT is inherited in three forms, i.e., autosomal dominant,

autosomal recessive and X-linked conditions. The specification fails to support an association of a mutation in periaxin with all the three forms of CMT.

In addition, the specification does not establish the identity of any specific critical nucleotide or amino acid alteration(s) that are associated with loss of function or are associated with myelinopathy. The missense mutations in table-2 were also found in unaffected controls. The specification does not teach if patients had one copy of mutation, or if they were homozygous or compound heterozygous for other mutations in periaxin. It is clear from the teachings in table-2, that the mere presence of an alteration in periaxin such as a substitution or deletion is not indicative of myelinopathy. Further, with regard to the 2145T-> A and 274Δ C mutation in claim 36, and the R196X, C715X, or R82FSX96, the specification has provided no data as to whether these mutations are even associated with myelinopathy. Since the specification has not identified any specific critical amino acid alteration, it is further unclear whether these mutations or any specific mutation will have a significant affect or not.

Quantity of Experimentation Necessary:

Given the lack of guidance in the specification and the unpredictability in the art, it would require a large amount of experimentation to practice the invention as claimed. Neither the art nor the specification provides the skilled artisan with a predictable correlation that any mutation in periaxin is significantly associated with any specific myelinopathy. To practice the invention as claimed, the skilled artisan would have to perform a large study of patients with different types of myelinopathy, such as CMT, DSS, and matched controls to determine if any general alteration or mutation in periaxin or any specific claimed alteration or mutation in periaxin, was associated with any specific myelinopathy. Such a study would consist of mainly trial and error

analysis, the outcome of which is clearly unpredictable as exemplified by the state of the art. Therefore, given the lack of guidance from the specification as to any statistical association between the claimed association of any mutation in periaxin polynucleotide and any myelinopathy, and the unpredictability taught in the art as to some point mutations in other genes such as PMP22 are associated with one form of CMT, while other mutations in the same PMP22 are associated with DSS, the skilled artisan would be required to perform undue experimentation to practice the invention as broadly as it is claimed.

10. With regard to the rejection made in the previous office action under 35 USC 112, first paragraph (enablement), the rejection is maintained and reiterated from the previous office action. Applicants amendment, arguments and declaration are fully considered and found not persuasive for the following reasons:

Amount of direction and guidance:

Applicants' argue that the instant specification provides an association between periaxin (PRX) mutations and myelinopathies and statistically significant association is not required to show a reasonable association. Applicants' further argue that the instant specification provides association of a variety of PRX mutations with the exemplary myelinopathy that is being recessive Dejerine-Sottas neuropathy. These arguments are fully considered and found not persuasive because the instant specification provides a specific set of mutations in PRX, demonstrates that only a specific type of such mutations are likely to be associated with a specific type of myelinopathy (DSN) but extrapolates that any and all mutations in PRX, including unkwown mutations and mutations which do not necessarily lead to an altered protein,

are associated with any type of myelinopathy. The specification does not support a correlation between any mutation in PRX and any general or specific myelinopathy.

Applicants' assert that the instant specification notes in paragraph (0005) that Gillespie et al. (2000) teaches association of periaxin with myelin sheath, thus a skilled artisan would recognize that it is not undue to demonstrate mutations in different myelinopathies by assaying a periaxin polynucleotide. This argument is fully considered and found not persuasive because Gillespie et al. teach a complete knockout of PRX gene (PRX -/-) would result in demyelinating disease. Gillespie et al. did not show that any mutation in PRX would result in demyelination. From the teachings of Gillespie et al., an ordinary artisan would recognize that a complete absence of PRX gene would result in demyelinating disease.

Applicants' also assert that the specification provides direction and guidance by providing definition for myelinopathy and disclosure of the spectrum of myelinopathies which include some specific types of myelinopathies (see page 13-14 of the applicants' response) and asserts that the disclosure is in compliance to the requirements of MPEP 2164.03 and any in-operable embodiments does not necessarily render them non-enabled or invalid. Applicants' arguments are fully considered and found not persuasive. The statute under 112 first paragraph requires that the scope of the claims be commensurate in scope with the teachings in the specification. In the instant case, the specification teaches PRX mutations which are not associated with myelinopathy in general (see paragraph 0244 on page 66, table 2 on page 67) or any of the specific myelinopathy in the claims, as such the teachings in the specification are not commensurate in scope with the claims.

Working examples and level of predictability:

Applicants' also argue that the specification provides a correlation between any mutation in PRX gene and any myelinopathy (spectrum of closely related diseases) or any specific myelinopathy and the inheritance patterns for myelinopathies are irrelevant. Applicants also point out that PRX mutations (2145>A and 247delC) are associated with peripheral neuropathy in general and assert that it identifies another genetic cause for CMT1 spectrum of myelinopathies. Applicants' also assert that the specification provides plenty of working examples to assist one of the skill in the art how to identify these alterations as disease causing in the diagnosis of specific myelinopathies. Applicants' arguments are fully considered and are not persuasive. First, the specification provides in example 8, an association of some specific PRX mutations with peripheral neuropathies and none of the mutations are specific for SEQ ID NO. 76. The specification in paragraph (0244) teaches unaffected parents and son of family HOU579 and two sisters and son of the patient HOU418 are heterozygous for PRX mutation. This indicates that the presence of two alleles with specific frameshift mutations is necessary for development of a specific peripheral neuropathy. Thus it is clear that not all mutations of PRX are associated with the broad spectrum of myelinopathies because patients with only a single allele mutation were not affected (see paragraph 0244 on page 66) would not result in myelinopathy in general. The specification fails to teach that all mutations of PRX, irrespective of mutation in a single allele or mutations in two alleles would lead to any type of myelinopathy.

The specification provides working examples that demonstrate that mutations in periaxin are not necessarily disease associated because

(i) only disease association was shown when 2 copies of PRX gene encode a specific protein truncation or frame shift mutation. However, the specification teaches that family

members who contained only one copy of the PRX gene with the specific mutation were not affected.

(ii) the specification teaches at page 67, table 2, that missense mutation occur in both control population as well as unaffected subjects. Therefore the specification shows that a number of mutations found in PRX gene are not disease associated. Thus the specification does not reasonably predict that any mutation in PRX is associated with any myelinopathy.

Applicants argue that undue experimentation standard can not be used to maintain the present rejection and assert that experimentation for associating particular nucleotide alterations with a specific myelinopathy and /or other nucleotide alterations with other myelinopathies within this same highly related group of afflictions would be routine and not undue. Applicants' assertions are fully considered and found not persuasive. The specification expressly teaches that certain mutations are not associated with any general or specific myelinopathy therefore it would take a large amount of trail and error analysis for the skilled artisan to determine which mutations are associated and are not associated with the disease. Given the unpredictability with associating PRX mutations and any general or specific nyelinopathy, as shown in the specification, such experimentation is considered undue. Thus the rejection is maintained herein.

11. With regard to the declaration submitted under 37 CFR 1.132, The declaration is fully considered and found not persuasive. As discussed above, the statute under 112 first paragraph requires that the scope of the claims be commesurate in scope with the teachings in the specification. In the instant case, the specification teaches some PRX mutations are not associated with myelinopathy in general (see paragraph 0244 on page 66, and table 2 on page 67) or any of the specific myelinopathy in the claims, but found in normal controls and unaffected

family members. As such the teachings in the specification are not commensurate in the scope with the claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 35-36, 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims 1 and 35 are confusing and unclear because the preamble of the claims does not agree with last positive step of the claims. The preamble recites intended use and the last positive step recites assaying said sample for an alteration in periaxin polynucleotide, which is not clear whether the method is to diagnose the myelinopathy or to assay a sample for an alteration in periaxin polynucleotide.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 2-3, 38, 44-45 and 50 are rejected under 35 U.S.C. 102(a) as being anticipated by Boerkoel et al. (Am. J. Hum. Genet. Vol. 68, pages 325-333, 2001).

Boerkoel et al. teach a method for diagnosing myelinopathy (Dejerine-Sottas Neuropathy- DSN) in an individual, wherein said myelinopathy resulted from a periaxin alteration, comprising

(i) obtaining a sample containing nucleic acid from said individual (see 326, column 1, paragraph 1 under the sub title subjects and methods);

(ii) assaying said sample for an alteration in a periaxin polynucleotide having 100% sequence homology with the instant SEQ ID NO. 76 (see page 326, column 2, paragraph 1 under sub title mutation screening, see attached sequence alignment). Thus the disclosure of Boerkoel et al. meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 5, 35, 39, 40, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gillespie et al. (Genomics, vol. 41, pages 297-298, 1997).

With regard to claim 1, Gillespie et al. teach a method for localizing periaxin gene in a sample, wherein the method comprises (i) obtaining a sample containing nucleic acid (see page

297, column 2, lines 3-15); (ii) assaying said sample to ascertain if any of the genetic markers are associated with periaxin (see page 297, column 2, lines15-22). Gillespie et al. also teach that the periaxin gene defects may underlie certain human peripheral neuropathies, which include Charcot-Marie-Thooth (CMT) (see page 297, column 1, paragraph 1); the said assaying comprises a polymerase chain reaction (see page 297, column 2, lines15-22); comparing the differences between the test nucleic acid (murine PRX gene) with a reference nucleic acid (human orthologues of Pkcc and D7Nds5) (see page 298, column 1, paragraph 1).

However, Gillespie et al. did not teach specifically assaying for an alteration in periaxin.

It would have been obvious to one skilled in the art to modify the method of assaying for periaxin as taught by Gillespie et al. to achieve a method for assaying for an alteration in periaxin because Gillespie et al. expressly taught that defects in periaxin protein may underlie certain human peripheral neuropathies since several forms of CMT type I, a peripheral demyelinating condition, have been shown to be caused by mutations in genes that expressed in myelinating Schwann cells (see page 297, column 1, paragraph 1). Gillespie et al. also taught that the periaxin co seggregates with human orthologue of Pkcc, PRKCC, which maps to human chromosome 19q13.4, that is syntenic with mouse chromosome 7 (see page 297, column 2, paragraph 1, page 298, column 1, paragraph 1). An ordinary skilled artisan would have been motivated to modify the method for assaying periaxin gene with the screening of mutations in periaxin gene because Gillepsie et al. taught mutations in periaxin may be associated with human peripheral neuropathies, therefore one skilled in the art would be motivated to look for mutations or alterations in preiaxin.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
April 27, 2004

JEHANNE SITTON
PRIMARY EXAMINER
4/27/04